DEPARTMENT OF HEALTH AND HUMAN SERVICES

NATIONAL INSTITUTES OF HEALTH

NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES

NATIONAL ADVISORY ALLERGY AND INFECTIOUS DISEASES COUNCIL

MINUTES OF MEETING

May 19-20, 1997

Building 31, Conference Room 10
National Institutes of Health
Bethesda, Maryland 20892

*Available from NIAID Committee Management Office

(301) 496-7601

PUBLIC HEALTH SERVICE
NATIONAL INSTITUTES OF HEALTH

NATIONAL ADVISORY ALLERGY AND INFECTIOUS DISEASES COUNCIL

MINUTES OF MEETING

May 19-20, 1997

The 126th meeting of the National Advisory Allergy and Infectious Diseases Council (NAAIDC) was convened at 8:30 a.m. on Monday, May 19, 1997 in Conference Rooms 8, 9 and 10, Building 31, National Institutes of Health. Dr. Anthony S. Fauci, Director of the National Institute of Allergy and Infectious Diseases (NIAID), presided as Chairman.

In accordance with the provisions of Public Law 92-463, the meeting was open to the public from 1:00 p.m. to 4:00 p.m. on May 19, and from 8:30 a.m. to 4:30 p.m. on May 20. The meeting was closed to the public on May 19 from 8:30 a.m. to 1:00 p.m. and again from 3:30 p.m. to 4 p.m., for review and consideration of individual grant applications. Notice of the meeting was published in the *Federal Register*.

Council Members Present:
Dr. Janet Butel
Dr. Robert Couch
Dr. Jerrold Ellner
Dr. Laurie Glimcher
Ms. Louise Jacobbi
Dr. Howard Johnson
Dr. Warren Johnson, Jr.
Mr. Stephan Lawton
Dr. Paula Pitha-Rowe
Ms. Orvalene Prewitt
Dr. Samuel Silverstein
Ms. Emily Spitzer
Dr. Judith Thomas
Dr. Lowell Young

Council Members Absent:
Mr. Martin Delaney
Mr. Garry Lyle
Dr. W. Gary Tarpley
Ms. Mildred Williamson

Ex Officio Member Present:
Dr. James Hughes, Centers for Disease Control and Prevention

Ex Officio Member Absent:
Dr. Fred Gordin, Veterans Administration

AIDS Research Advisory Committee, NIAID Members Present:
Dr. Gary Nabel
Dr. Charles Rinaldo
Mr. Ryland Roane
Dr. Cladd Stevens

Ex Officio & Liaison Members of ARAC Present:
Dr. Harold Jaffe
Dr. Norman Letvin

***Ad Hoc* Members Present**:
Dr. Paul Allen
Dr. Charles Janeway, Jr.
Dr. Marc Jenkins
Dr. Stanley Lemon
Dr. John Mekalanos
Dr. Kenneth Rock

NIAID Staff Attending:
Dr.. Elizabeth Adams, Special Assistant to the Director, DAIT
Ms. Kristin Adamson, Program Specialist, DAIT
Ms. Diane Adger-Johnson, Technical Information Specialist, PAB
Dr. Jeffrey Albert, Mathematical Statistician, BRB, DAIDS
Dr. Margaret Ashworth, Chief, CSMB, TRP, DAIDS
Dr. Kathryn Aultman, Vector Biology Program Officer, PIPB, DMID
Dr. Phillip J. Baker, Lyme Disease Program Officer, BMB, DMID
Mr. Todd Ball, Chief, MGMS, GMB, DEA
Ms. Patricia Baron, Biologist, OSC, DAIDS
Ms. Mabel Battistone, Head, RSU, DEA
Dr. Fred Batzold, Chief, CSMB, TRP, DAIDS
Dr. Christopher Beisel, Persisting Viral Infections Program Officer, VB, DMID
Ms. Diana Berard, Technical Assistant, EDHB, DMID
Mr. Steven Berkowitz, Associate Director for Management and Operations
Dr. Roberta Black, Microbiologist, TIB, BSP, DAIDS
Dr. William Blackwelder, Chief, Biometry Branch, DMID
Mr. John Bowersox, OC, NIAID
Dr. James Bradac, Microbiologist, PRB, VPRP, DAIDS
Ms. Teri Brown, Technical Information Specialist, PAB
Dr. Kerri Burton-Danner, Intern, DMID
Mr. Lawrence Butler, Contract Officer, CMB, DEA
Dr. Kevin Callahan, Scientific Review Administrator, AITRC, MIRB, SRP, DEA
Ms. Sarah Carr, Director, OPA
Dr. Scott Cairns, Senior Scientist, TIB, PBRB, DAIDS
Ms. Anne Claysmith, Health Specialist, OSC, DAIDS

Dr. Pamela Clax,, Health Specialist, TRP, DAIDS
Ms. Carole Cole, Health Specialist, CSMB, TRP, DAIDS
Dr. Elaine Collier, Chief, AS, CIB, DAIT
Dr. Janet Connolly, Chief, GTB, DAIT
Ms. Janet Cordell, Nurse Clinical Coordinator, CSS, CRAB, DMID
Dr. George Curlin, Deputy Director, DMID
Mr. Allan Czarra, Director, Office of Program Coordination and Operations Branch, DEA
Dr. Lawrence Deyton, Acting Director, DEA
Dr. Howard Dickler, Chief, CIB, DAIT
Dr. Carl Dieffenbach, Associate Director, BSP, DAIDS
Dr. Dennis M. Dixon, Chief, BMB, DMID
Ms. Ann Doane, Program Assistant, OPSI, DAIDS
Ms. Laura Doepel, Technical Writer/Editor, OC
Dr. Patricia D'Souza, Health Scientist Administrator, BSP, OD, DAIDS
Dr. William Duncan, Associate Director, TRP, DAIDS
Ms. Laura Eisenman, DAIT Coordinator, Grants Management Specialist, GMB, DEA
Dr. Patricia Fast, Associate Director, VPRP, DAIDS
Dr. Jorge Flores, Medical Officer, VPRP, DAIDS
Dr. Mary Glenn Fowler, Deputy Branch Chief, ETB, VPRP, DAIDS
Dr. Lawrence Fox, Medical Officer, HIVRB, TRP, DAIDS
Ms.Thelma Gaither, Cytokine and Antiviral Clinical Trials Program Officer, DMID
Dr. Bruce Gellin, Medical Officer, CRAB, DMID
Dr. Vassil Georgiev, Scientific Review Administrator, APRRB, SRP, DEA
Dr. Ann Ginsberg, Tuberculosis, Leprosy, and Other Mycobacteria Diseases Program Officer, RDB, DMID
Dr. Michael Gottlieb, International Tropical Diseases and Parasite Biology Program Officer, PIPB, DMID
Dr. Mark Grabowsky, Chief Medical Officer, ETB, VPRP, DAIDS
Dr. Charles Hackett, Chief, Molecular and Structural Immunology Section, BIB, DAIT
Dr. B. Fenton Hall, Host Immunity Program Officer, PIPB, DMID
Ms. Molly Hardison, Program Analyst, OPA
Ms. Gail Havely-Aly, Program Coordinator, DAIDS
Dr. Carole Heilman, Associate Director for Scientific Program Development, DAIDS
Dr. Milton J. Hernandez, Director, OSTMD, DEA
Dr. Stephen Heyse, Medical Bacteriology and Antibacterial Resistance Program Officer, BMB, DMID
Ms. Phyllis Hill, Program Coordinator, DAIT
Dr. Penelope J. Hitchcock, Chief, STDB, DMID
Dr. Rodney Hoff, Chief, ETB, VPRP, DAIDS
Ms. Jacqueline Holden, Contracting Officer, APRCS, CMB, DEA
Dr. Hortencia Hornbeak, Director, Scientific Review Program, DEA
Dr. Jill Horowitz, Virology Program Officer, STDB, DMID
Dr. Dominick Iacuzio, Influenza and Related Viral Respiratory Diseases Program Officer, RDB, DMID
Dr. Peter Jackson, Chief, AIDS, CERRB, SRP, DEA
Ms. Gail Ginsburg Jacobs, Tuberculosis Technical Assistant, RDB, DMID
Dr. Leslye Johnson, Chief, EDHB, DMID
Ms. Susan Jones, RSU, DEA
Dr. Jonathan Kagan, Chief, DDCSB, DAIDS

Ms. Deborah Katz, Director, OPOSI, DAIDS
Dr. John Y. Killen, Director, DAIDS
Dr. Jane Kinsel, Assistant Director for Special Projects, OD, DMID
Ms. Mary Kirker, Chief, Grants Management Branch, DEA
Dr. David Klein, Bacterial Respiratory Diseases l Program Officer, RDB, DMID
Ms. Joan Kondratick, Biologist, OSC, DAIDS
Ms. Toni Kuhn, Chief, AIDS PRCS, CMB, DEA
Ms. Marilyn Kunzweiler, Administrative Officer, EAMB
Dr. John La Montagne, Director, DMID
Dr. Chris Lambros, Microbiology, OIRB, TRP, DAIDS
Ms. Sarah Landry, Program Analyst, OPOSI, DAIDS
Dr. Dennis Lang, Bacterial and Viral Enteric Diseases Program Officer, EDHB, DMID
Dr. Catherine Laughlin, Chief, VB, DMID
Dr. Barbara Laughon, Chief, OIRB, TRP, DAIDS
Dr. Dale Lawrence, Chief Medical Officer for Vaccine Science, ETB, VPRP, DAIDS
Ms. Wendy Liffers, Deputy Associate Director for Management and Operations
Dr. Charles Litterst, Section Chief, DDCSB, TRP, DAIDS
Ms. Daniella Livnat, Health Specialist, DDCSB, DAIDS
Mr. Edward Lucas, RSU, DEA
Dr. Bonnie Mathieson, OAR
Mr. Paul Marshall, Program Analyst, OPA
Ms. Diane Martin, Budget Analyst, FMB
Ms. Elaine Matzen, Health Specialist, ETB, VPRP, DAIDS
Ms. Marybeth McClauley, Health Specialist, ETB, VPRP, DAIDS
Dr. John McGowan, Deputy Director, NIAID
Mr. Paul McFarlane, Contract Specialist, CMB, DEA
Dr. Pamela McInnes, Chief, RDB, DMID
Dr. James McNamara, Chief, PMB,TRP, DAIDS
Dr. Nancy Miller, Microbiologist, PRB, VPRP, DAIDS
Dr. Gregory Milman, Chief, PBRB, DAIDS
Dr. Paolo Miotti, Epidemiologist, EB, DAIDS
Ms. Theresa Mizell, Program Coordinator, DMID
Ms. Judy Murphy, Deputy Director, OC
Dr. Mohamed Nasr, Chemist, DDCSB, TRP, DAIDS
Ms.Blanche O'Neill, Health Specialist, VPRP, DAIDS
Ms. Diane Parris, Administrative Officer, EAMB
Dr. Estella Parrott, Coordinator of Research Programs, ORMWH, OD, NIAID
Ms. Mary Parsons, Health Specialist, OD, DMID
Dr. Marshall Plaut, Chief, AMS, AAIB, DAIT
Ms. Maureen Power, Nurse Consultant, OIRB, TRP, DAIDS
Dr. Lawrence Prograis, Deputy Director, DAIT
Dr. Helen Quill, Chief, BIB, DAIT
Dr. Robert Quackenbush, Assistant Director for Training, Referral, and Minority Affairs, DMID
Dr. M. Sayeed Quraishi, Scientific Review Administrator, ACERRB, SRP, DEA
Dr. Regina Rabinovich, Chief, Clinical Studies Section, CRAB, DMID
Ms. Sahira Rafiullah, Deputy Director, OPA
Ms. Merilee Rahe-Stoline, Contract Specialist, CMB, DEA

Dr. Wasima Rida, Statistician, BRB, DAIDS
Dr. Stephen Rose, Chief, GTB, DAIT
Dr. Zeda Rosenberg, Senior Science, ETB, VPRP, DAIDS
Dr. Daniel Rotrosen, Acting Director, DAIT
Dr. Fran Rubin, Respiratory Diseases Program Officer, RDB, DMID
Dr. Polly Sager, Director, Office of Scientific Coordination, DAIDS
Dr. Leigh Sawyer, Clinical Trials Program Officer, VB, DMID
Dr. Steve Schnittman, Assistant Director for Clinical Research, TRP, DAIDS
Dr. Lewis Schrager, Chief, EB, BSP, DAIDS
Dr. Alan Schultz, Chief, PRB, VPRP, DAIDS
Ms. Justina Schwemberger, Research Training Officer, OSTMD, DEA
Ms. Linda Scott, Legislative Analyst, OPA
Dr. Vicki Seyfert, Chief, Immunoregulation Section, BIB, DAIT
Dr. Opendra Sharma, Health Scientist Administrator, PBRB, DAIDS
Ms. Rona Siskind, Program Analyst, OPSI, OD, DAIDS
Dr. Sharilyn Stanley, Special Assistant for Science Policy, OD, NIAID
Ms. Jo Ann Stesney, Program Analyst, OPCO, DEA
Dr. Christopher Taylor, Bacterial Respiratory Diseases II Program Officer, RDB, DMID
Ms. Eveline Tierney, IND Coordinator, CRAB, DMID
Dr. Dianne Tingley, Chief, APRRB, SRP, DEA
Ms. Carolyn Tolbert, Deputy Chief, PAB
Dr. Christopher Tseng, Antiviral Research and Antimicrobial Chemistry Program Officer, VB, DMID
Ms. Marilyn Tuttleman, Technical Assistant, BMB, DMID
Ms. Jane Unsworth, Grants Management Specialist, AIDS Division Coordinator, GMB, DEA
Mr. Mark VanRaden, Statistician, BB, DMID
Dr. Mary Clare Walker, Microbiologist, CDB, VPRP, DAIDS
Dr. Karl Western, Assistant Director for International Research, NIAID
Mr. Thomas Williams, Budget Officer, NIAID
Ms. Virginia Wilson, CMA, CMO, DEA
Ms. Jeannie Wood, Health Specialist, CSMB, TRP, DAIDS
Ms. Melanee Woodard, Grants Financial Analyst, FMB
Dr. Janet Young, Biologist, PBRB. BSP, DAIDS

NIH Staff Attending:
Dr. Mark Guyer, NCHGR
Dr. Betty J. Hayden, DRG
Dr. Clifford Lane, DIR/CC
Dr. Calbert D. Liang, DRG
Dr. Bruce Maurer, DRG
Dr. Sam A. Mayyasi, DRG
Dr. Gilbert Meier, DRG
Dr. Nabeeh Mourad, DRG
Dr. Walter Schaffer, OD/OER
Dr. David Simpson, DRG
Ms. LaVerne Stringfield, NIH/CMO
Ms. Patricia Turner, NINDS
Dr. Eugene Zimmerman, DRG

Others:
Ms. Nancy Carter-Foster, Department of State
Dr. Dolph Chianchiano, National Kidney Foundation
Dr. Jacquelynne Corey, AAOA
Dr. James Dickson, Harvard Medical School
Ms. Anita Dopkosky, McKesson Bioservices
Ms. Brenda Wood Frances, Mayatech Corp.
Ms. Linda Gage-White, American Academy of Otolaryngology
Ms. Maureen Hannley, American Academy of Otolaryngology
Ms. Cheryl Hayden, American Academy of Dermatology
Dr. Maryanna Henkart, National Science Foundation
Dr. Michele Hogan, AAI
Mr. Kiyoshi Kuromiya, Critical Path AIDS Project
Mr. Dan Lucey, Office of Vaccines, FDA
Mr. Preston Marx, Aaron Diamond AIDS Research Center
Mr. Michael J. Morgan, The Wellcome Trust
Ms. Pamela Moore, Capitol Publications
Dr. Lynn Morrison, American Social Health Association
Dr. Georgia Persinos, Washington Insight
Dr. Michael Saag, University of Alabama at Birmingham
Ms. Lisa Seachrist, BioWorld Today
Ms. Nicole Sobotka, American Lung Association
Ms. Lisa White, The Blue Sheet
Mr. Steven Wakefield, The Night Ministry

I. REVIEW OF GRANT APPLICATIONS - (Closed to the Public)

The National Advisory Allergy and Infectious Diseases Council convened in closed session on Monday afternoon, May 19, to consider applications en bloc in the areas of allergy and immunology, microbiology and infectious diseases, and AIDS.

Pending Actions: The Council reviewed 743 research and training applications with primary assignment to NIAID for a requested amount of $733,194,155 in first-year direct costs and recommended approval of 694 applications for $608,688,721 in first-year direct costs. Four Method to Extend Research in Time (MERIT) awards were recommended for approval.

II. REMARKS OF THE DIRECTOR, NIAID - Anthony S. Fauci, M.D.

Dr. Fauci opened the Monday afternoon, May 19, session of Council by welcoming visitors to the 126th meeting. He welcomed the ad hoc Council members: Dr. Paul Allen, Professor of Pathology, Washington University; Dr. Charles Janeway, Jr., Professor of Immunobiology, Yale University;
Dr. Marc Jenkins, Associate Professor, Department of Microbiology, University of Minnesota Medical School; Dr. Stanley Lemon, Professor and Chair, Department of Microbiology and Immunology, University of Texas Medical Branch at Galveston; Dr. John Mekalanos, Professor and Chair, Department

of Microbiology and Molecular Genetics, Harvard Medical School; and Dr. Kenneth Rock, Professor and Chairman, Department of Pathology, University of Massachusetts Medical Center.

A. Consideration of Minutes of Previous Meeting: The minutes of the January 23-24, 1997 meeting were considered and approved as written.

B. Dates of Future Council Meetings: September 8-9, 1997; and for 1998, February 2-3, June 1-2 and September 24-25.

C. Staff and Organizational Changes:

Within the Office of the Director, NIAID, Dr. John McGowan has been appointed Deputy Director of the Institute. In this position Dr. McGowan will provide leadership for scientific policy issues, and oversee the Office of Communication, and the Office of Research on Minority and Women's Health. Mr. Steven Berkowitz has been appointed Associate Director for Management and Operations. In this role he will assist the Institute Director with the overall management and operations of the Institute, and oversee the offices of Administrative Services, Financial Management, Technology Transfer, Human Resources, Policy Analysis, and Technology Information Systems.

Dr. Fauci announced the recruitment process has begun to fill the position of Director, Division of Extramural Programs (DEA). Dr. Lawrence Deyton has served in an outstanding capacity as the Acting Director of DEA and will continue in the position until a new Director is appointed.

Dr. Fauci announced the departure of Dr. Robert Goldstein, who left the Directorship of the Division of Allergy, Immunology and Transplantation (DAIT) to become Vice President for Research at the Juvenile Diabetes Foundation International. Dr. Daniel Rotrosen has been appointed to serve as the Acting Director of DAIT while a national search is conducted for a new Director.

Within the Division of Microbiology and Infectious Diseases (DMID), Ms. Martha Mattheis, Chief of the Clinical and Regulatory Affairs Branch (CRA), has retired after almost 30 years service with NIAID. Dr. George Curlin, Deputy Director, DMID is currently serving as Acting Branch Chief, CRA.

D. Budget Update:

For both this year and next, the NIH budget news is good. This fiscal year, NIAID raised its paylines to the 26.0 percentile for AIDS and 24.0 for non-AIDS. The payline for FIRST grants (R29) is the 32.0 percentile for both AIDS and non-AIDS research. Intramurally, NIAID is benefiting from $5 million in AIDS vaccine money from the Office of AIDS Research.

Though the President requested a 2.6 percent increase for the NIH, Congress is pushing for more money for FY 1998, as much as 7.5 percent over the FY 1997 funding level. If this occurs, NIAID will reduce the level of programmatic reductions and increase the cap on type 2 (recompeting) awards - both good news for grantees. Under this scenario, percentile-based reduction bands would be as low as 5, 7, and 9 percent versus the current 17, 19, and 21 percent. For recompeting applications, NIAID would allow grantees to request as much as 20 percent more money than they received in the last year of their previous grant, up from the current cap of 10 percent.

E. Legislative Update:

NIAID participated in a successful round of congressional hearings. At Council, Dr. Fauci described his experience testifying before the House Appropriations Subcommittee in February, "Chairman Porter and the Subcommittee Members have been extremely generous to and supportive of NIAID and NIH research, and it was a pleasure to testify before them."

Members of Congress have shown interest in these NIH-related areas:
Protease inhibitors
AIDS vaccine - roles of Congress, NIH and industry
Malaria research
Impact of the media on research
Cloning
Gulf War syndrome

F. Other:

NIAID/NCI Intramural Vaccine Center

As announced by President Clinton in May, NIH has begun developing a Vaccine Research Center to focus on AIDS vaccines. The new center will be part of the NIH intramural research program, a joint venture of the National Cancer Institute (NCI) and NIAID. It will stimulate multidisciplinary research from basic and clinical immunology and virology through vaccine design and production.

Resources will be provided by the NCI and the NIAID with FY 1998 funds from the Office of AIDS Research, which has proposed $10 million - $5 million to each Institute. A search committee will conduct a nationwide search for a director.

The Center will begin as a "laboratory without walls" while laboratory space is sought near the NIH Bethesda campus. Later, as scientists are recruited from outside, NIH will consider constructing a building on the campus for the Center.

Malaria

To tackle the increasing urgency of global malaria, NIAID is enlarging its investment in malaria research. Malaria kills two to three million people each year making it the most deadly tropical disease. NIAID has developed a research plan for expanded malaria research, produced by staff scientists with input from the international malaria research community. Focusing on the development of a malaria vaccine, the plan was recently reviewed and endorsed by an NIAID-sponsored blue ribbon panel.

The plan capitalizes on the Institute's commitment to malaria research and its track record in developing new vaccines. A growing body of research suggests that effective malaria vaccines are feasible. Success relies on applying a better understanding of the biology of malaria parasites and the human immune response to infection to vaccine development.

NIAID spends $19.2 million on malaria research, growing to about $21 million with the addition of the three new projects. Other research related to the plan will be funded as high-quality applications are received. The new malaria projects are to 1) establish a repository of well-characterized malaria reagents to improve access to research materials for investigators worldwide; 2) expand parasite genome sequencing to include the genomes of *Plasmodium vivax* and *Plasmodium falciparum*, which cause human malaria, and *Plasmodium berghei*, which causes malaria in rodents, providing an animal model for studying the disease; and 3) expand malaria vaccine production and evaluation through collaborations between intramural and extramural scientists.

HIV Vaccine Committee

As Dr. Fauci told Council, "The AIDS Vaccine Research Committee is in high gear." The committee, chaired by Dr. David Baltimore, explored prime-boost and live attenuated strategies for vaccine development at its second meeting in May; and in early March, the Committee held its first focus group meeting in Boston.

At the Boston meeting, an interdisciplinary group of experts in HIV and related areas discussed gaps and opportunities, including immune correlates and cell receptors, as well as three vaccine approaches: live attenuated, DNA, and envelope-based.

Together with the Committee, NIAID is trying to jump start the HIV vaccine field with the Innovation Grant Program for Approaches in HIV Vaccine Research. This program announcement (PA) supports high-risk or novel research in vaccine design and evaluation. NIAID will fund about $6 million in grant awards later this year. The first phase focuses on the HIV envelope, animal models, and antigen processing.

The response to the PA was strong. By the May 23 receipt date, NIAID had received over 130 applications. If the program accomplishes its goal of stimulating novel research, it may be extended to include other areas of scientific need related to HIV vaccine development.

Committee Reports

Dr. Glimcher reported on the Office of AIDS Research Advisory Committee meeting held in March. Among the many topics the Committee discussed was the need to improve the regional primate research centers, the need to make repositories and databases more user-friendly, the need for more research into AIDS pathogenesis, the involvement of AIDS patients in real-time studies, the need for more prevention studies, the lack of formulations of antiretrovirals suitable for young children, and the need to integrate clinical trials efforts within NIAID.

NIAID Office of Communications

The NIAID Office of Communications provided Council members with several publications and press releases. Dr. Fauci noted one publication in particular entitled "Emerging Infectious Disease Research: Meeting the Challenge." The publication provides a valuable lay language description of the Institute's emerging diseases research agenda.

III. UPDATE ON NIAID MANAGED CARE WORKING GROUP - Lawrence Deyton, M.D. Acting Director, Division of Extramural Activities, NIAID

Dr. Deyton gave Council an update on NIAID's working group on managed care, charged with estimating the impact of managed care on our scientific mission and identifying possible collaborations with managed care organizations. The group talked with intramural and extramural scientists to understand their concerns and begin to define potential opportunities in working with managed care organizations.

The group then formulated the following recommendations centered on engaging in pilot collaborations between NIAID-funded scientists and either public or private managed care organizations.

- Implement clinical trial referral agreements NIH is currently working out with the Department of Defense.

- Discuss possible collaborations between clinical investigators sponsored by NIAID (e.g., pediatric and adult AIDS Clinical Trials Group, Inner-City Asthma Centers) and state Medicaid programs.

- Initiate discussions with one or two large managed care organizations to stimulate patients referrals for NIAID's research programs.

- Support a small amount of research associated with ongoing projects to explore the impact of managed care on NIAID-supported basic research, clinical trials, and training.

IV. NIAID'S INTRAMURAL EFFORTS IN CLINICAL RESEARCH THROUGH TELEMEDICINE - Steven Holland, M.D., Senior Clinical Investigator, Laboratory of Host Defenses, Division of Intramural Research, NIAID

Dr. Holland showed NIAID's use of telemedicine technology as a collaborative effort between NIAID and South Texas Hospital in research on treating multi-drug tuberculosis. Telemedicine gives physicians the opportunity to look directly at a patient and data at a remote location. Working with Dr. Teresa Lightner and a volunteer patient in Texas, Dr. Holland showed images of a patient's tympanic membrane, retina, skin, and other laboratory and research technologies, which he and Council examined using this technology. They also discussed other available technologies and the scope and progress of the use of these technologies in research.

V. REPORT OF DIVISION OF ALLERGY, IMMUNOLOGY, AND TRANSPLANTATION COUNCIL SUBCOMMITTEE - Daniel Rotrosen, M.D., Acting Director, DAIT

It was with regret that NIAID announced the departure of Dr. Robert Goldstein, who served as Director of the Division of Allergy, Immunology and Transplantation since 1988. Dr. Goldstein has joined the Juvenile Diabetes Foundation International as Vice President for Research. In his new position, Dr. Goldstein will be responsible for developing and guiding the research agenda of the Foundation.

Dr. Goldstein began his career at NIAID in 1978 when he assumed the position of Chief of the Allergy and Clinical Immunology Branch in the Immunology, Allergic and Immunologic Diseases Program. As Director of this Division he has guided its scientific programs for close to a decade, and has been an effective and tireless proponent of collaboration in science. His ability to bring diverse groups and interests together toward a common goal is well-recognized. His extensive activities with private foundations as well as professional and lay organizations have led to important and innovative partnerships between the public and private organizations.

Effective March 13, Dr. Fauci has appointed Dr. Daniel Rotrosen to serve as the Acting Director. Dr. Rotrosen joined the NIAID in 1984, working first in the Laboratory of Clinical Investigation, Division of Intramural Research and later as a Medical Officer in the Laboratory of Host Defense. In 1995, he was appointed Chief of the Asthma, Allergy and Inflammation Branch in this Division. He received his M.D. from Boston University School of Medicine, and trained in internal medicine and infectious diseases at Harbor-UCLA Medical Center. He also served on the faculty of UCLA before coming to NIAID. Dr. Rotrosen has a long-standing interest in the basic mechanisms of inflammation and has published extensively on this topic.

Elizabeth Adams, M.D., recently joined the Division as Special Assistant to the Director. She came to NIAID from the Division of Intramural Research at the National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS) where she worked on the genetics of hereditary muscle diseases and on clinical myositis studies. Dr. Adams received her clinical rheumatology training at Washington University where she worked on the cloning and structure-function relationship of complement receptors in the laboratory of Dr. John Atkinson.

Dr. Rotrosen related the following scientific activities:

Asthma Center Directors Meeting. The bi-annual meeting of the NIAID Asthma Center Directors was held at NIH on April 17-18, 1997. This meeting was cosponsored by the NIAID, the National Institute of Environmental Health Sciences, and the National Heart, Lung and Blood Institute. The meeting highlighted recent progress of the many clinical and basic research programs that are cofunded by NIAID, NIEHS and NHLBI, including the National Cooperative Inner-City Asthma Study, the Collaborative Study for the Genetics of Asthma, and projects of the Asthma Centers. Participants in the meeting included representatives of various constituency groups, private and public foundations, the Environmental Protection Agency, the Centers for Disease Control and Prevention, and the New York City Department of Health.

Food Allergy Research. An executive summary of the workshop, "New Directions in Food Allergy Research," held at NIH in July, 1996, will be published in the July, 1997 issue of The Journal of Allergy and Clinical Immunology. This workshop focused on basic immune mechanisms, immune mechanisms in the gastrointestinal tract, characterization of allergens, and promising new advances in understanding the immunologic basis of allergic disorders. The workshop was sponsored by the Jaffe Family Foundation, the American Academy of Allergy, Asthma and Immunology, the International Life Sciences Institute and the NIAID.

Workshop on Sarcoidosis and on Immunologic Lung Diseases. NIAID is planning to hold a two-day workshop in September, 1997. This workshop will review new advances in understanding basic immune mechanisms, immune mechanisms in the respiratory tract, and the application of these observations to understanding the pathophysiology and treatment of sarcoidosis and other immunologic lung diseases. The workshop will also highlight areas of scientific opportunity and identify promising directions for future research.

American Association of Immunologists (AAI) Annual Meeting, San Francisco, February 21-26, 1997. The thirteenth annual Symposium on Contemporary Topics in Immunology was cosponsored by NIAID, AAI and the Clinical Immunology Society and chaired by Drs. Helen Quill, Paul Kincade and Arnold Levinson. This year's symposium included a presentation by the 1996 Nobel Laureate, Dr. Peter Doherty, on the immune control of gamma-herpes virus infections, as well as presentations on antigen transport across mucosal epithelia, the role of Fas-ligand in mediating immune privilege and the first crystal structures of the TCR and TCR-MHC-antigen complexes.

The NIAID and AAI cosponsored a workshop on grantsmanship and programs for under-represented minority investigators and students chaired by Drs. Quill, Robert Goldstein, Olivia Preble and Richard Goldsby.

NIAID and Bristol Meyers Squibb co-sponsor a trial of to prevent chronic kidney graft rejection. The NIAID-supported Cooperative Clinical Trial in Adult Transplantation and Bristol Meyers Squibb have agreed to co-sponsor a clinical trial to determine if an angiotensin-converting-enzyme inhibitor will prevent (Irbesartin®) chronic rejection. Bristol Meyers Squibb has agreed to supply the Irbesartin® and Pravastatin® for the trial and NIAID is performing all data analysis and patient recruitment in conjunction with its ongoing adult kidney transplant trials.

Xenotransplantation
There will be a scientific meeting July 21-22, 1997 at the Pooks Hill Marriott in Bethesda entitled "CROSS-SPECIES INFECTIVITY AND PATHOGENESIS". This meeting will bring together experts in viral and bacterial infectivity to discuss specific issues related to the ability of infectious agents to cross species barriers and cause disease. Members of the Infectious Disease Society of America, American Society of Microbiology, the American Society of Tropical Medicine and Hygiene, the Food and Drug Administration and the Centers for Disease Control and Prevention, as well as members of the NIAID Division of Microbiology and Infectious Diseases and Division of AIDS have been consulted about the agenda and speakers.

Diabetes Prevention Trial - Type 1 Launches Oral Trial
The Diabetes Prevention Trial-Type 1 (DPT-1), a large nation-wide multi-center clinical trial, is testing whether insulin, used as an immunotherapy, will prevent or delay the development of diabetes mellitus in first degree relatives of patients with Insulin Dependent Diabetes Mellitus (IDDM). This is the first large scale clinical trial of antigen-based intervention for the prevention of an autoimmune disease is funded by the National Institute of Diabetes and Digestive and Kidney Diseases, NIAID, National Institute of Child Health and Human Development, the Juvenile Diabetes Foundation International, and the American Diabetes Association.

Arthritis Research Conference
NIAID is co-sponsoring with the National Institute of Arthritis and Musculoskeletal and Skin Diseases, the Arthritis Foundation, and the American College of Rheumatology, the Arthritis Research Conference on May 29-June1, 1997. This conference will discuss major themes underlying contemporary arthritis research, including genetics, gene regulation, molecular immunology, and signaling. The meeting is designed to promote interactions between trainees and senior scientists and to stimulate new initiatives and foster collaborative interactions.

Workshop on Systemic Vasculitis
NIAID has received funds from the NIH Office of Rare Diseases to organize a workshop on Systemic Vasculitis. Examples include polyarteritis nodosa, Wegener's granulomatosis, microscopic polyangiitis, giant cell arteritis, and Takayasu's arteritis. This workshop (scheduled for September 15, 1997) will convene a group of experts in vasculitis, inflammation, and immunology to evaluate current investigations and advise NIAID on future directions for research in this area.

ANNOUNCEMENTS AND SOLICITATIONS

REQUEST FOR PROPOSALS (RFP) - PRIMARY IMMUNODEFICIENCY DISEASE REGISTRY
NIAID issued a Request for Proposals to support a five year program to establish and maintain a registry of clinical information on U.S. residents affected by primary immunodeficiency diseases. This project is based on the success of the existing registry for chronic granulomatous disease and the recommendations of a workshop which was convened by NIAID and the NIH Office of Rare Diseases to discuss the utility of a registry for additional primary immunodeficiency diseases.

CURRENT RESEARCH AND FUTURE DIRECTIONS: IMMUNOLOGICAL BASIS FOR VACCINES
Ad hoc Council members and guests presented their current research efforts in the area of immunological basis for vaccines: Moderator, Dr. Charles Hackett, National Institute of Allergy and Infectious Diseases (NIAID), Section Chief, Molecular and Structural Immunology, Basic Immunology Branch, DAIT introduced speakers and topics: Dr. Charles Janeway, Yale University: **Setting the Stage for an Effective Immune Response**; Dr. Paul Allen, Washington University: **Antigenic Antagonism as a Cause of Vaccine Failure**; Dr. Marc Jenkins, University of Minnesota: **Memory Cell Induction, Maintenance, and Triggering**; Dr. Jonathan Yewdell, Laboratory of Viral Diseases, NIAID: **Epitope Immunodominance and its Role in Vaccine Design**; Dr. Kenneth Rock, University of Massachusetts: **Antigen Presenting Cells, Antigen Processing Pathways and Antigen Targeting**; Dr. Mary Ann Robinson, Laboratory of Immunogenetics, NIAID: **Human Genetics of Immune Responsiveness to Vaccines**. Dr. Patricia Fast, Division of Acquired Immune Deficiency Syndrome (DAIDS) and Dr. Regina Rabinovich, Division of Microbiology and Infectious Diseases (DMID), NIAID presented: **Perspectives on Vaccines.**

CONCEPT REVIEW
One proposed research emphasis area was presented, discussed and approved.

Basic and Clinical Research on Immune Tolerance: This NIAID-wide initiative would promote multidisciplinary, interactive research focused on the understanding and/or application of antigen-specific immune tolerance mechanisms. Projects that combine basic science with clinical research will be of special

interest. The objectives are: (1) to promote a more complete understanding of the basic mechanisms responsible for inducing and maintaining immune tolerance in an antigen-specific manner, (2) to facilitate translation of experimental knowledge on immune tolerance into clinical therapies for the treatment or prevention of immune-mediated disease, and (3) to promote more effective development of vaccines by preventing pathogen-induced immune tolerance.

VI. REPORT OF THE JOINT MEETING OF AIDS SUBCOMMITTEE, NAAIDC, AND AIDS RESEARCH ADVISORY COMMITTEE, NIAID - John Y. Killen, M.D., Director, DAIDS

The meeting, which was held in the Natcher Conference Center on the campus of the National Institutes of Health, was chaired by Dr. Gary Nabel, chairman of the AIDS Research Advisory Committee (ARAC).

Report from the Director — Dr. John Y. Killen

Dr. Killen welcomed Committee members and others attending the meeting and thanked them for their participation. He first addressed the NIAID FY 1997 budget, in which pay lines have been raised for both AIDS and non-AIDS research. The President's budget request for FY 1998 included a 4.4 percent increase for NIAID, the highest of all NIH Institutes, Centers, and Divisions (ICD's). In comparison, NIH received a 2.6 percent overall increase. NIAID's high percentage increase is explained by the fact that NIAID projects reflect current priorities, even for non-AIDS research. The AIDS research increase for NIAID is 4.7 percent, higher than AIDS research increases allotted to other ICD's. Important AIDS initiatives to be pursued in 1998 include the Strategic Program for Innovative Research on AIDS Vaccines, Basic Research on Mucosal Immune Response to HIV Vaccines, Acute Infection and Early Disease Research Program, and International Trials on Prevention of Perinatal HIV Transmission.

Dr. Killen noted that the Congressional budget may allot more funds to NIH, and, if so, the funding plan will be modified.

Dr. Killen mentioned President Clinton's recent announcement of the goal to achieve an HIV vaccine within 10 years. To help achieve this goal, a vaccine center is being established to consolidate all NIH intramural vaccine research activities. This initiative will bring scientists together who are already working on HIV vaccines. He also indicated that growth in the NIH AIDS budget will be preferentially channeled into vaccine research and development, both extramural as well as intramural research. Some of the 1998 NIAID budget initiatives reflect this.

Dr. Killen congratulated Dr. William Duncan on receiving the Department of Health and Human Services 1997 Secretary's Award for Distinguished Service from Secretary Shalala.

Dr. Killen reviewed the recent controversy concerning NIH and CDC supported studies of interventions to disrupt perinatal transmission in developing countries. The watchdog group, Public Citizen, criticized these studies as being unethical because they did not include the antiretroviral regimen that was shown to be effective in the 076 study. Dr. Killen stated, however, that Public Citizen is confusing a standard of care issue with an ethical issue and is not considering the reality of health care in the developing world, where simpler interventions are needed. He noted that the countries in question want and need interventions that are easier to administer and less expensive. They, in fact, requested assistance with these trials and have been involved in every aspect of their planning and conduct. Dr. Killen indicated that DAIDS has received many strong letters of support and that the Institute stands behind the trials.

Dr. Killen next provided information on program activities. A factsheet was prepared and widely disseminated to respond to questions about the program announcement for the Centers for AIDS Research (CFAR). Language in the announcement was revised to clarify that two separate CFAR's can utilize one resource site if there is a demonstrated need.

A working group is being convened to prepare for the recompetition of the AIDS Clinical Trials Group (ACTG) and the Terry Beirn Community Programs for Clinical Research on AIDS (CPCRA). In keeping with the recommendations of the Levine Report, the working group will examine various options for integrating the efforts of these two clinical trials networks. An NIH task force, consisting of group leadership, independent scientists and NIH staff will define the specifications of an integrated clinical trials system, while NIAID will focus on the renewal of the CPCRA and ACTG and the structure of the RFAs. In addition, the Office of AIDS Research will be creating an overarching therapeutic research advisory group.

Dr. Killen updated the Committee on status of DATRI 002, the low dose oral alpha interferon (LDOAI) study. Although the ARAC recommended that the NIAID undertake this study to obtain reliable data on the effects of LDOAI, the study has not progressed as planned. Low patient accrual, high drop-rates, and problems with data quality have hampered the study. The study team and the Division of AIDS have worked together to try to address these issues, but it is apparent that community interest in the study has waned. The data and safety monitoring board (DSMB) will assess the study's enrollment and data quality later this month and could recommend closing the study if these problems have not improved.

Dr. Killen thanked outgoing committee members Mr. Ryland Roane and Dr. Gary Nabel for their years of service on the ARAC and their significant contributions. He presented each with a certificate of appreciation..

Vaccine and Prevention Research Program
Vaccine Trials: Status Update — Dr. Patricia Fast
Dr. Fast prefaced her remarks on NIAID vaccine trials by stating that fundamental research underlies all vaccine design and evaluation. She outlined the vaccine design and evaluation process, from preclinical research to parallel animal model research and Phase I/II clinical research (to compare animal and human data) through to the efficacy study. Vaccines are designed to prevent viral entry, prevent viral replication, or destroy infected cells. Multiple vaccine concepts must be carried out because no one approach is known to work best. Concepts being pursued include those for vaccines composed of peptides, subunit envelopes, recombinant particles, whole-killed HIV, DNA, and live-attenuated SIV and HIV.

The AIDS Vaccine Evaluation Group (AVEG) is conducting 25 Phase I trials and 1 Phase II trial, with 15 vaccine candidates, to compare safety and immune responses. The larger HIVNET (HIV Network for Prevention Trials) is conducting trials in the United States and abroad. Dr. Fast summarized the clinical trials being carried out on peptides, envelope proteins, vaccinia/canarypox, prime-boost approach, canarypox, and virus-like particles. Mucosal vaccines are being actively investigated. She noted that researchers are striving to find a vaccine that provides a broad response from which the virus cannot escape.

Vaccine Education: What Next? — Mr. Steve Wakefield

Mr. Wakefield opened by showing several minutes of an educational videotape, "No Easy Answers," aimed at potential participants in the HIVNET 014/AVEG 202, prime-boost vaccine trial. Several committee members commented on the excellence of the film. He discussed the challenges facing the national community advisory board (CAB), which was established, in part, to facilitate community education, outreach and recruitment efforts.

Mr. Wakefield described six educational tools designed by HIVNET's Community Education and Media Relations Committee and NIAID for persons considering volunteering for the prime-boost trial: (1) a booklet explaining vaccines, (2) slides describing social harms, (3) top 10 questions and answers, (4) the above-mentioned videotape, (5) NIAID fact sheets, and (6) a guide to informed consent. The committee's membership includes national staff, site staff, community educators, and community members. Mr. Wakefield noted that community members requested education about the informed consent process.

Mr. Wakefield next listed four important areas for community education to be addressed by the CAB: (1) allowing for different opinions, (2) how to inform the community about avoiding the errors of the Tuskegee study, (3) providing materials appropriate for diverse gender and ethnic groups, and (4) assessing community readiness for a Phase III trial. Mr. Wakefield remarked that the gay press rarely addresses HIV vaccines.

AIDS Vaccine Research Committee — Dr. Carol Heilman

Dr. Heilman reported on the activities of the AIDS Vaccine Research Committee (AVRC), chaired by David Baltimore, Ph.D. The AVRC was recently established to assist NIH in developing a comprehensive research program to expedite discovery and development of an AIDS vaccine. Its first meeting took place in February 1997.

AVRC is charged with enhancing current NIH AIDS vaccine programs by reviewing scientific opportunities, gaps in knowledge, and future directions of research. Vaccine designs to be reviewed include peptide-based vaccines, protein-based vaccines, vector-based vaccines, DNA vaccines, live-attenuated virus vaccines, and killed virus particles, including virus-like particles. To identify and address needs for vaccine concept development, AVRC will consider structure/function studies of Env protein, antibody response, mucosal immunity, cellular immunity, animal models, and human immunology. The committee is addressing the definition of "vaccine research," availability of primate resources, coordination of U.S. and international efforts, and maximum utilization of the NIH clinical infrastructure to further vaccine development. Empirical research into prime-boost, DNA, and live-attenuated virus vaccines is particularly emphasized. Basic research areas to be stressed are viral pathogenesis, structure/functions, and modes of immune response.

Dr. Heilman described AVRC's first recommendation, the new INNOVATION Grant Program for Approaches in HIV Vaccine Research. This program was developed by NIAID with input from the scientific community. It supports research projects that may be highly innovative and involve risk. Grant applications were due on May 23.

Discussion areas were the constituency of nationwide focus groups being convened to assist AVRC, the role of AVRC in the NIH infrastructure, and the importance of human clinical studies in vaccine research.

Chemoprophylaxis: Scientific Update and Research Opportunities — Dr. Preston Marx, Dr. Brooks Jackson, and Dr. Michael Saag

Dr. Killen introduced this section of the program by stating that DAIDS is considering future research initiatives in chemoprophylaxis. Several investigators were invited to address the committee to facilitate a discussion of potential opportunities for concomitant basic research on the biology of HIV infection.

First, Dr. Marx discussed the applicability of a macaque animal model to chemoprophylaxis research. He listed areas where researchers now have choices: multiple routes of exposure (intravenous, mucosal, intramuscular/subcutaneous), varying pathogenicity of infecting stock, varying tropisms of challenge stock, infected cells in different mucosal and lymphoid tissues, and varying outcome/endpoints. A key problem in the use of monkeys is dosage—oral formulations are more available but are not easily adapted to the animal model. Oral dosages must be administered by stomach tube several times daily, which is a strain on the animals and also expensive. Injection formulations are preferred, and subcutaneous injection is the route of choice. Dr. Marx then provided an overview of macaque SIV research that is applicable to HIV chemoprophylaxis research. He described vaginal and rectal transmission models, target cell research (the dendritic cell is thought to be the first target cell), and a penile urethra transmission model. He explained that SIV typically develops more rapidly than HIV. He noted that SIV and HIV have been found to use different T-cell receptors. Several laboratories are studying the unidentified SIV receptor, and results are expected soon.

Dr. Jackson then reviewed chemoprophylaxis research on prevention of perinatal transmission in humans. Perinatal transmission is a serious problem worldwide: half of the 26 million HIV-infected people in the world are women of child-bearing age, and 300,000 to 600,000 HIV-positive children are born each year. Dr. Jackson described research being conducted in Uganda, where seroprevalence rates in women were found to average 31 percent. About 26 percent of HIV-infected mothers passed the virus to their newborn children. Dr. Jackson stressed that many factors can affect calculations of these rates. Routes of viral transmission are intrauterine, intrapartum, and through breast-feeding. The intrapartum route is thought to be the most common. Potential interventions include chemoprophylaxis of pregnant mothers to reduce viral load during the prenatal period, vaginal washing as well as chemoprophylaxis at the time of delivery, and postnatal chemoprophylaxis of the mother and infant. Some methods, particularly use of AZT, have been more successful than others. Several international trials are under way that are modifying AZT regimens. An exciting new effort is investigating chemoprophylaxis of the mother and infant with nevirapine; data are showing powerful antiviral activity. Cost and toxicity aspects of this drug also appear favorable.

Finally, Dr. Saag discussed the possibility of early intervention with chemoprophylaxis to prevent acute HIV infection. His particular interest is the biology of the immune response at the time of initial infection. He described the notion of a "set point"— an equilibrium stage between the immune response to exposure and replication of the virus. When an exposure takes place, a few cells become "activated," enough to initiate an immune response. At this point, however, no major cell replication has started. How the immune system responds to the viral challenge might affect whether infection proceeds.
Dr. Saag then listed several areas of pathogenesis and mechanism of infection to consider for future research: repeated exposure as a risk factor for likelihood of infection, inoculum, natural protection, cell tropism, receptors, and concomitant sexually transmitted diseases. A number of clinical and behavioral issues must also be considered.

Following the three presentations, the Committee discussed the feasibility of tying basic research into ongoing chemoprophylaxis studies to learn about the stage between HIV exposure and infection. Many opportunities were noted, although they also noted several significant logistical, ethical, cost, and technological issues.

IL-2 Update — Dr. H. Clifford Lane and Dr. Lawrence Fox
Dr. Lane provided a brief overview of interleukin-2 (IL-2) therapy for HIV infection. He reviewed recent findings from several trials documenting substantial increases in CD4+ T cells. He listed the main side effects, which include fatigue, malaise, myalgia, and headache. He also presented results comparing subcutaneous and intravenous modes of administration showing that subcutaneous administration is equally effective. In conclusion, he stated that a Phase III efficacy trial is needed to prove that IL-2 yields clinical as well as laboratory benefit in humans.

Dr. Fox reviewed the progress to date on initiating a Phase III trial of IL-2. In January 1997, DAIDS convened a multinational group of investigators interested in exploring the possibility of conducting a Phase III trial. The group reviewed the available Phase II data and agreed that a Phase III clinical efficacy trial of IL-2 for therapy of HIV disease should be developed. Several pilot trials are planned internationally to test the safety and practicality of conducting a Phase III trial at new clinical sites. On May 19, 1997, DAIDS held a meeting of the international Phase III collaborators, where data from ongoing studies were presented. The group formulated a protocol structure and discussed potential accrual issues, including patient retention. Other issues to resolve include logistics, regulation, resources, ethics, and antiretroviral therapy. Meanwhile, European and Canadian investigators are determining the interest of their colleagues in the trial. A protocol executive committee meeting is proposed for July, to be held in Italy. The trial steering committee will meet again to finalize protocol development, no later than September 1997.

In discussion after the IL-2 presentations, Committee members mentioned the toxicity of the drug as well as its potential benefit to patients in early versus more advanced stages of disease.

FY 1999 Initiatives: Concept Reviews

Concept Review: DAIDS Specimen Repository — Ms. Elaine Matzen
This initiative proposes the continuation of a centralized repository, which stores, catalogs, and retrieves specimens collected from participants in domestic and international clinical research studies sponsored by DAIDS. It provides an infrastructure for delivery of specimens to research groups and individual investigators for collaborative HIV/AIDS studies. Committee members discussed issues related to user access, specimen quality control, and retention procedures. They approved the concept with the modification that a management plan addressing prioritization of specimen collection and storage be developed before issuance of the RFP.

Concept Review: Immunology Quality Assessment Program — Ms. Daniella Livnat
This initiative provides for the continuation of this program, whose objective is to provide a flexible resource for standardization and quality control of immunologic assays used in multisite HIV investigations. The program has accomplished a specific objective of monitoring and certifying laboratories for testing CD4+ T cell and other lymphocyte subsets. Its current objectives are to (a) support comparative evaluations of novel cytometric instruments, methods, and reagents, and (b) facilitate standardization, validation, and quality assessment of immunological assays for implementation in multicenter investigations. The committee approved the concept with the following modifications: an advisory committee should be established; the relationship between the contractor and the immunology investigators should be strengthened to support efficient assay development; an evaluation component should be added; and the contract should have the potential to acquire a broad range of quality control materials, in addition to whole blood.

Concept Review: Research Support Services Contract — Ms. Vaurice Starks
This initiative provides for continuation of operational and logistical support for three large prospective epidemiological cohort studies within DAIDS: the Multicenter AIDS Cohort Study (MACS), Women and Infants Transmission Study (WITS), and Women's Interagency HIV Study (WIHS). The contract's objective is to enhance coordination and communication within the three studies through management and administrative support, conference and teleconference support, and provision of research resources. The committee approved the concept.

VIII. REPORT OF THE DMID COUNCIL SUBCOMMITTEE - John La Montagne, Ph.D. Director, DMID

Dr. John R. La Montagne, Ph.D., Director of the Division of Microbiology and Infectious Diseases (DMID), welcomed the Microbiology and Infectious Diseases Subcommittee of the National Advisory Allergy and Infectious Diseases Council and provided a brief report of Division activities. He thanked the *ad hoc* Subcommittee members Drs. Stanley Lemon and John Mekalanos. He also noted personnel and organizational changes since the last meeting.

Dr. La Montagne mentioned several activities in connection with the U.S.-Japan Cooperative Medical Science Program. A new Panel on Acute Respiratory Infections has been established; the first meeting was held in March in Japan. A successful second conference on emerging infectious diseases was held in Bangkok in March; a summary of the meeting will be published soon. Finally, there have been discussions concerning collaborative studies of *Escherichia coli* 0157 under the aupices of the Cholera and Related Diarrheal Diseases Panel; a workshop to discuss and develop specific proposals for collaborative efforts to address this emerging health problem will be held in Baltimore in June.

Program staff presented updates on four coordinated, collaborative clinical and pre-clinical trials groups which focus on the development and testing of new and improved therapeutic and vaccine measures: the Collaborative Antiviral Study Group, the Collaborative Antiviral Testing Group, the Mycoses Study Group, and the Vaccine Treatment and Evaluation Units.

The Biometry Branch presented information about its organization structure and research activities and solicited comments from the Subcommittee on their stated goals and future directions.

Malaria in Africa Activities. In the context of the global importance of malaria and the Institute's long-standing commitment to research on this disease, Dr. Michael Gottlieb of the Parasitology and International Programs Branch discussed recent activities in this area. Specifically he reviewed the events leading up to the NIH co-sponsored International Conference on Malaria in Africa which was held in Dakar, Senegal in January 1997. That meeting brought together malariologists from the US, Europe and Africa to discuss the challenges and opportunities in malaria research needed to improve malaria control and to enhance the capacity of African scientists to conduct research. Dr. Gottlieb summarized the major scientific recommendations from the meeting including: 1) the need for improved communication in Africa (access to electronic communication and the Internet); 2) networking to study malaria in different epidemiological settings; and 3) establishment of repositories of malaria-related resources (parasite isolates, human samples; mosquito vectors, molecular and immunological reagents, *etc.*). Representatives from a number of public and private agencies which support biomedical research also attended the Dakar meeting and they considered a number of approaches to coordinate their activities and to increase funding for malaria

research. Dr. Gottlieb indicated that the NIAID and NIH was actively engaged in this process and that a follow-up meeting of research funding agencies and others was scheduled for July in the Hague to further this effort.

The Council recognized the importance of these activities on a disease of great public health importance and they applauded the efforts undertaken thus far. Council looked forward to learning more about these activities especially about specific plans and initiatives under consideration by NIAID and by NIH.

Emerging Diseases. Dr. La Montagne presented an overview of DMID-activities related to emerging diseases and acknowledged that this continues to be a very active area for DMID. One challenge, given that resources are finite, is how to focus involvement in consortiums and collaborations with other agencies in the US and with other countries to produce tangible outcomes while managing very complex research programs.

Training. Dr. Robert Quackenbush, DMID, and Dr. John Bennett, DIR, presented material related to the DMID training program. Included was a summary of the review of the DMID training program by a panel of extramural scientists and presentation of their recommendations. Council discussed and enthusiastically supported these recommendations. One suggestion was to consider whether a coordinated institute oversight approach might permit better management of complex, multi-disciplinary research training.

Hepatitis C. Dr. Leslye D. Johnson, Chief of the Enteric and Hepatic Diseases Branch, provided an update on hepatitis C. The increasing importance of this viral infection as well as prevention and intervention status were highlighted. Current DMID activities including the new Hepatitis C Cooperative Research Centers (HC CRCs) and antiviral trial capabilities through the Collaborative Antiviral Study Group were presented as well as a brief summary of the recent NIH Consensus Development Conference on "Management of Hepatitis C". DMID recently initiated discussions with outside experts to develop a research-based approach for progress on hepatitis C. Subcommittee members heard about: 1) DMID's current approaches, 2) the key needs such as access to defined clinical populations and the chimpanzee animal model as well as the development of suitable model systems, and 3) new opportunities like an infectious clone developed by one of the HC CRC investigators. Dr. Johnson summarized the research questions in the areas of transmission, host immune response, pathogenic mechanisms and natural history, and viral replication and therapy strategies which were defined with the help of the outside experts. Council members inquired further into the status of research and development. They believed that the approach was outstanding and that the key research areas provided definition and stimulus for future scientific investigation.

Pathogen Genome Sequencing. Recent advances in sequencing DNA and in bioinformatics have enabled investigators to rapidly sequence the entire genomes of microorganisms, including those of human pathogens. Dr. Michael Gottlieb reviewed the NIAID's extensive support of bacterial genome sequencing projects. In addition, he articulated the benefits of this research for the improved understanding of pathogen biology and of host-pathogen interactions as well as for the development of diagnostics, drugs and vaccines. Dr. Gottlieb summarized the contributions of NIAID in the multiagency effort to sequence the entire genome of *Plasmodium falciparum*, the most lethal malaria parasite.
Dr. Michael Morgan of the Wellcome Trust, the other major public funder of pathogen genome sequencing projects, reviewed the Trust's activities in this area, including their efforts to develop a "consortium" of public agencies and of pharmaceutical companies to sequence a larger number of pathogens of clinical and public health importance.

Following these reviews of ongoing activities, Dr. Ann Ginsberg of the Respiratory Diseases Branch presented a number of issues which are confronting the Institute with regard to these genome sequencing projects. Specifically, Dr. Ginsberg indicated that there are issues regarding: 1) project solicitation and the mechanism of their support; 2) the nature of review by an IRG; 3) the possibility of duplication of effort; 4) data release policies and intellectual property rights; and, 5) interactions with other agencies. Council members recognized the significance of these genome sequencing projects and their great potential. However, Council members also recognized the importance of the issues and concerns raised by Dr. Ginsberg and indicated that more time was needed to discuss them. Council adjourned without a clear set of recommendations and entrusted the Institute to further develop plans to deal with the concerns raised.

VIII. ADJOURNMENT

The meeting of the Council was adjourned at 4:30 p.m. on Tuesday, May 20, 1997

Monday, May 19, 1997, 8:30 a.m. - 4:00 p.m.
Tuesday, May 20, 1997, 8:30 a.m. - 4:30 p.m.

We do hereby certify that, to the best of our knowledge, the foregoing minutes are accurate and complete.

Anthony S. Fauci, M.D. ***July 28, 1997***
Anthony S. Fauci, M.D. Date
Chairman, National Advisory Allergy
and Infectious Diseases Council
Director, National Institute of Allergy
and Infectious Diseases

Lawrence Deyton, M.D. *July 24, 1997*
Lawrence Deyton, M.D. Date
Acting Executive Secretary
National Advisory Allergy and Infectious
Diseases Council
Acting Director, Division of Extramural Activities
National Institute of Allergy and Infectious
Diseases

These minutes will be formally considered by the Council at its next meeting; any corrections or notations will be incorporated in the minutes at the meeting.